Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Idecabtagene vicleucel (Abecma®)	MP-RX-FP-111-23	☒ MMM MA ☒ MMM Multihealth

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Part B Drug

Service Description

This document addresses the use of Idecabtagene vicleucel (Abecma®), a B-cell maturation antigen (BCMA)-directed genetically modified autologous T cell immunotherapy approved by the Food and Drug Administration (FDA) for the treatment of adult patients with relapsed or refractory multiple myeloma after four or more prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody.

Background Information

In the United States, multiple myeloma accounted for approximately 1.8% (32,270) of new cancer cases and about 2.1% (12,830) of cancer-related deaths in the year 2020, as reported by the National Institutes of Health (NIH) in 2021. This condition represents a rare form of blood cancer characterized by the abnormal accumulation of plasma cells in the bone marrow, leading to the development of tumors in multiple bones throughout the body. Moreover, multiple myeloma disrupts the bone marrow's ability to generate a sufficient number of healthy blood cells, resulting in reduced blood counts. The disease can also manifest as bone and kidney damage, as well as a compromised immune system. It is important to note that multiple myeloma currently lacks a cure and is marked by alternating periods of remission and relapse.

Abecma (idecabtagene vicleucel) is a first-in-class CAR-T cell therapy with B-cell maturation antigen (BCMA)-targeting single-domain antibodies for individuals with multiple myeloma. Abecma works by binding to the BCMA protein, which is widely expressed on malignant plasma cells in multiple myeloma, leading to cancer cell death. . It was approved with breakthrough therapy and orphan drug designations by the FDA. The FDA's decision to grant approval was grounded in the efficacy and safety data of the pivotal Phase II KarMMa trial.

The KarMMA study by Munshi and colleagues (2021) was an open-label, single-arm, multicenter trial involving 128 adult patients with relapsed and refractory multiple myeloma (RRMM) who had previously undergone a minimum of three lines of antimyeloma therapy, including treatment with an immunomodulatory agent, proteasome inhibitor, and an anti-CD38 monoclonal antibody. Patients were administered target doses of idecabtagene vicleucel ranging from 150 to 450 million CAR-positive T cells. 95% of patients were refractory to an anti-CD38 monoclonal antibody, with 88% of these individuals having undergone four or more prior lines of therapy, and 85% being triple-class refractory, meaning they were resistant to a proteasome inhibitor (PI), an immunomodulatory drug (IMiD), and an anti-CD38 monoclonal antibody. Efficacy measurements were based on the primary endpoint of overall response (partial response or better) and a key secondary endpoint of complete response or better (including complete and stringent complete responses). After a median follow-up duration of 13.3 months, it was found that 73% (94/128) of patients displayed a response, while 33% (42/128) achieved a complete response or better. Safety findings from the study indicated that neutropenia occurred in 91% (117/128)

of patients, anemia in 70% (89/128) of patients, and thrombocytopenia in 63% (81/128) of patients. Additionally, cytokine release syndrome (CRS) was observed in 84% (107/128) of patients, and neurologic toxicities (NT) were reported in 18% (23/128) of patients.

According to a study by Delforge and colleagues (2022), ide-cel exhibited robust and long-lasting responses in patients with relapsed and refractory multiple myeloma (RRMM) who had been exposed to three or more classes of therapies in the KarMMa Trial. These researchers conducted an investigation into the health-related quality of life (HRQoL) of the KarMMa trial participants, using the European Organization for Research and Treatment of Cancer Quality of Life C30 Questionnaire and its supplementary 20-item multiple myeloma module, along with the EuroQol 5-dimension 5-level instrument. These assessments were carried out at various time points, including screening, baseline (within 72 hours before or on the same day as lymphodepletion), the day of ide-cel treatment, and after ide-cel treatment. Clinically meaningful changes in HRQoL, exceeding pre-established thresholds, were considered.

Out of the 128 patients treated with ide-cel in the KarMMa Trial, 126 (98%) were included in the HRQoL analysis. The RRMM burden at the baseline, before treatment, was notably high and worse compared to the age- and sex-adjusted general population. However, statistically significant and clinically meaningful improvements in various HRQoL parameters were observed. These improvements included a reduction in pain (-8.9) and disease symptoms (-10.2) by month 1, as well as a decrease in fatigue (-7.2), enhanced physical functioning (6.1), improved cognitive functioning (6.7), and a better global health status/quality of life (8.0) by month 2. The most pronounced enhancements in fatigue, pain, and physical functioning were seen at months 9, 12, and 18, respectively, and they were maintained over a 15 to 18-month period following ide-cel treatment. The authors concluded that for patients with RRMM who had been exposed to three or more classes of therapies and had limited treatment options and a poor prognosis, a single infusion of ide-cel resulted in early, sustained, statistically significant, and clinically meaningful improvements in HRQoL.

Abecma has a black box warning for cytokine release syndrome (CRS), and should not be administered in patients with active infection or inflammatory disorders due to risk of life-threatening reactions and death. Severe or life-threatening CRS should be treated with tocilizumab with or without corticosteroids. Abecma also has black box warning for causing neurological toxicities, which could also be severe and life-threatening. Monitoring for neurological events after administration is recommended. Additionally, there are black box warnings for hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS), including fatal and life-threatening reactions, and warnings regarding prolonged cytopenias with bleeding and infection, including fatal outcomes. Due to these black box warnings, Abecma is only available through a Risk Evaluation and Mitigation Strategy (REMS) program.

Definitions and Measures

- Allogeneic cells: Harvested from a histocompatible donor. Autologous cells: Harvested from the individual's own cells.
- Bone marrow: A spongy tissue located within flat bones, including the hip and breast bones and the skull. This tissue contains stem cells, the precursors of platelets, red blood cells, and white cells.

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- Chemotherapy: The medical treatment of a disease, particularly cancer, with drugs or other chemicals. Chimerism: Cell populations derived from different individuals; may be mixed or complete.
- Complete Response (CR): The disappearance of all signs of cancer as a result of treatment; also called complete remission; does not indicate the cancer has been cured.
- Cytotoxic: Treatment that is destructive to cells, preventing their reproduction or growth.
- ECOG or Eastern Cooperative Oncology Group Performance Status: A scale and criteria used by doctors and researchers to assess how an individual's disease is progressing, assess how the disease affects the daily living abilities of the individual, and determine appropriate treatment and prognosis. This scale may also be referred to as the WHO (World Health Organization) or Zubrod score which is based on the following scale:
    - 0 = Fully active, able to carry on all pre-disease performance without restriction
    - 1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, for example, light house work, office work
    - 2 = Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours
    - 3 = Capable of only limited self-care, confined to bed or chair more than 50% of waking hours
    - 4 = Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair
    - 5 = Dead
- Hematopoietic stem cells: Primitive cells capable of replication and formation into mature blood cells in order to repopulate the bone marrow.
- Line of Therapy:
    - First-line therapy: The first or primary treatment for the diagnosis, which may include surgery, chemotherapy, radiation therapy or a combination of these therapies.
    - Second-line therapy: Treatment given when initial treatment (first-line therapy) is not effective or there is disease progression.
    - Third-line therapy: Treatment given when both initial (first-line therapy) and subsequent treatment (second-line therapy) are not effective or there is disease progression.
- Refractory Disease: Illness or disease that does not respond to treatment.
- Relapse or recurrence: After a period of improvement, during which time a disease (for example, cancer) could not be detected, the return of signs and symptoms of illness or disease. For cancer, it may come back to the same place as the original (primary) tumor or to another place in the body.

Approved Indications

The FDA approved indication for Abecma is for the treatment of adult patients with relapsed or refractory multiple myeloma after four or more prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody.

Other Uses

None

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Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS	Description
Q2055	Q2055-Idecabtagene vicleucel, up to 460 million autologous b-cell maturation antigen (bcma) directed car- positive t cells, including leukapheresis and dose preparation procedures, per therapeutic dose.

ICD-10	Description
C90.00	Multiple myeloma not having achieved remission
C90.02	Multiple myeloma in relapse
Z51.12	Encounter for antineoplastic immunotherapy

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Medical Necessity Guidelines

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Idecabtagene vicleucel (Abecma®)

A. Criteria For Initial Approval

i. Individual is 18 years of age or older; **AND**
ii. Individual has a diagnosis of relapsed or refractory multiple myeloma; **AND**
iii. If individual has a history of an allogeneic stem cell transplant, there are no signs of active graft versus host disease (GVHD);

AND

iv. Individual has adequate bone marrow reserve defined by *all* of the following:
   A. Absolute neutrophil count (ANC) ≥ 1000 cells/uL; **AND**
   B. Platelet count ≥ 50,000 cells/uL; **AND**
v. Individual has an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 1; **AND**
vi. Individual has not received prior treatment with CAR T-cell or B-cell maturation antigen (BCMA) targeted therapy;

AND

vii. Individual is using as a one-time, single administration treatment.

B. Criteria For Continuation of Therapy

i. Further treatment with Abecma will not be authorized since it is designated for a single-dose administration as per its indication.

C. Authorization Duration

i. Initial Approval Duration: 3 months (1 dose only, tocilizumab (Actemra) will be approved if requested)
ii. Reauthorization Approval Duration: Not applicable

D. **Conditions Not Covered**

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

i. Repeat administration; **OR**
ii. Active presence or history of central nervous system involvement with myeloma; **OR**

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iii. Presence or history of plasma cell leukemia; **OR**
iv. Individual has solitary plasmacytomas or non-secretory myeloma without other evidence of measurable disease; **OR**
v. Using in combination with other chemotherapy agents (not including the use of lymphodepleting chemotherapy prior to infusion); **OR**
vi. If prescribe in combination with other CAR T-cell immunotherapy (e.g. Breyanzi, Carvykti, Kymriah, Tecartus, Yescarta); **OR**
vii. Individual has active GVHD; **OR**
viii. History of chimeric antigen receptor therapy or other genetically modified T-cell therapy; **O**
ix. History of cardiac conditions, such as New York Heart Association (NYHA) stage III or IV congestive heart failure, myocardial infarction or coronary artery bypass graft (CABG) within the past 6 months, history of clinically significant ventricular arrhythmia or unexplained syncope, not believed to be vasovagal in nature or due to dehydration, or history of severe non- ischemic cardiomyopathy; **OR**
x. Left ventricular ejection fraction (LVEF) less than 45% (scan performed ≤ 8 weeks of leukapheresis); **OR**
xi. Active hepatitis B, active hepatitis C, human immunodeficiency virus (HIV) positive, or other active, uncontrolled infection; **OR**
xii. When the above criteria are not met, and for all other indications.

Limits or Restrictions

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

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Drug	Recommended Dosing Schedule
Idecabtagene vicleucel (Abecma®)	The recommended dose range is 300 to 460 x 106 CAR-positive T cells.

Additional Dosing Information

- Idecabtagene vicleucel (Abecma) is designated for autologous administration via intravenous infusion solely within a certified healthcare setting. Each dose of Abecma comprises a cell suspension containing 300 to 460 million CAR-positive T cells
- Abecma is provided as a single dose for infusion containing a suspension of chimeric antigen receptor (CAR)-positive T cells in one or more infusion bags.
- **Pretreatment**: Abecma should be initiated 2 days after completing lymphodepleting chemotherapy regimen with cyclophosphamide 300 mg/m^2/day intravenously (IV) and fludarabine 30 mg/m^2/day IV for 3 days. Abecma administration should be delayed in patients who experience unresolved serious adverse events (especially pulmonary events, cardiac events, or hypotension), including those after preceding chemotherapies; or active infections or inflammatory disorders.
- **Premedication** should include acetaminophen (650 mg orally) and diphenhydramine (12.5 mg IV or 25 to 50 mg orally, or another H1-antihistamine) approximately 30 to 60 minutes before infusion of Abecma. Prophylactic use of dexamethasone or other systemic corticosteroids should be avoided, as the use may interfere with the activity of Abecma.
- **Post-medication**: Tocilizumab plays an important role in the treatment of patients receiving CAR T-cell therapy such as Abecma. It manages and mitigates cytokine release syndrome (CRS), which can occur after CAR T-cell infusion. Tocilizumab should be available to the patient prior to infusion and during the recovery period.

Reference Information

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3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2022; Updated periodically.
5. Munshi NC, Anderson LD, Shah N, et al. Idecabtagene Vicleucel in Relapsed and Refractory Multiple Myeloma. N Engl J Med. 2021 Feb 25;384(8):705-716. doi: 10.1056/NEJMoa2024850.
6. NCCN Clinical Practice Guidelines in Oncology™. © 2022 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on October 5, 2022.
7. Multiple Myeloma. V1.2023. Revised September 14, 2022.

8. NCT033617848. ClinicalTrials.gov. U.S. National Library of Medicine. Available https://clinicaltrials.gov/ct2/show/NCT03361748?term=NCT03361748&draw=2&rank=1.
9. Protocol for: Munshi NC, Anderson LD Jr, Shah N, et al. Idecabtagene vicleucel in relapsed and refractory multiple myeloma. N Engl J Med 2021;384:705-16. DOI: 10.1056/NEJMoa2024850. Available at: https://www.nejm.org/doi/suppl/10.1056/NEJMoa2024850/suppl_file/nejmoa2024850_protocol.pdf
10. Raje N, Berdeja J, Lin Y, et al. Anti-BCMA CAR T-Cell Therapy bb2121 in Relapsed or Refractory Multiple Myeloma. N Engl J Med. 2019;380(18):1726-1737. doi:10.1056/NEJMoa1817226. Available at: https://www.nejm.org/doi/full/10.1056/NEJMoa1817226.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

Policy History

Revision Type	Summary of Changes	P&T Approval Date	MPCC Approval Date
Policy Inception	Adopted from Elevance Medical Policy	N/A	12/22/2023

Revised: 11/28/2023